

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
4 January 2001 (04.01.2001)

PCT

(10) International Publication Number
WO 01/00615 A1(51) International Patent Classification⁷: C07D 401/14,
A61K 31/4709, 31/4375, 31/437, 31/498, 31/4409,
31/436, A61P 11/00, 31/12, C07D 471/04, 417/14, 413/14,
409/14, 401/06, 491/056

(21) International Application Number: PCT/EP00/05677

(22) International Filing Date: 20 June 2000 (20.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 99202089.1 28 June 1999 (28.06.1999) EP

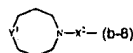
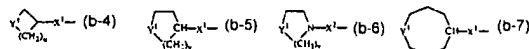
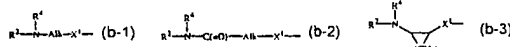
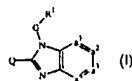
(71) Applicant (for all designated States except US):
JANSSEN PHARMACEUTICA N.V. [BE/BE]; Turn-
houtseweg 30, B-2340 Beerse (BE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): JANSSENS,
Frans, Eduard [BE/BE]; Janssen Pharmaceutica N.V.,
Turnhoutseweg 30, B-2340 Beerse (BE). LACRAMPE,Jean, Fernand, Armand [FR/FR]; Janssen-Cilag S.A.,
1, rue Camille Desmoulins, TSA 91003, F-92787
Issy-les-Moulineaux Cedex 9 (FR). GUILLEMONT,
Jérôme, Emile, Georges [FR/FR]; Janssen-Cilag S.A.,
1, rue Camille Desmoulins, TSA 91003, F-92787
Issy-les-Moulineaux Cedex 9 (FR). VENET, Marc,
Gaston [FR/FR]; Janssen-Cilag S.A., 1, rue Camille
Desmoulins, TSA 91003, F-92787 Issy-les-Moulineaux
Cedex 9 (FR). ANDRIES, Koenraad, Jozef, Lodenwijk,
Marcel [BE/BE]; Janssen Pharmaceutica N.V., Turnhout-
seweg 30, B-2340 Beerse (BE).(74) Agent: QUAGHEBEUR, Luc; Janssen Pharmaceutica
N.V., Patent Department - 3547, Turnhoutseweg 30,
B-2340 Beerse (BE).(81) Designated States (national): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE,
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,
NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

[Continued on next page]

(54) Title: RESPIRATORY SYNCYTIAL VIRUS REPLICATION INHIBITORS



(57) Abstract: The present invention concerns compounds of formula (I), prodrugs, *N*-oxides, addition salts, quaternary amines, metal complexes and stereochemically isomeric forms thereof wherein $-a^1=a^2=a^3=a^4-$ represents a radical of formula $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$; $-\text{N}=\text{CH}-\text{CH}=\text{CH}-$; $-\text{CH}=\text{N}-\text{CH}=\text{CH}-$; $-\text{CH}=\text{CH}-\text{N}=\text{CH}-$; $-\text{CH}=\text{CH}-\text{CH}=\text{N}-$; wherein each hydrogen atom may optionally be substituted; Q is a radical of formulae (b-1), (b-2), (b-3), (b-4), (b-5), (b-6), (b-7) and (b-8), wherein Alk is C_{1-6} alkanediyl; Y¹ is a bivalent radical of formula $-\text{NR}^2-$ or $-\text{CH}(\text{NR}^2\text{R}^4)-$; X¹ is NR^4 , S, S(=O), S(=O)₂, O, CH₂, C(=O), CH(=CH₂), CH(OH), CH(CH₃), CH(OCH₃), CH(SCH₃), CH(NR^{5a}R^{5b}), CH₂-NR⁴ or NR⁴-CH₂; X² is a direct bond, CH₂, C(=O), NR⁴, C_{1-6} alkyl-NR⁴, NR⁴- C_{1-6} alkyl, t is 2 to 5; u is 1 to 5; v is 2 or 3; and whereby each hydrogen in Alk and in (b-3), (b-4), (b-5), (b-6), (b-7) and (b-8), may optionally be replaced by R³; provided that when R³ is hydroxy or C_{1-6} alkyloxy, then R³ cannot replace a hydrogen atom in the α position relative to a nitrogen atom; G is a direct bond or optionally substituted C_{1-10} alkanediyl; R¹ is an optionally substituted bicyclic heterocycle; R² is hydrogen, formyl, C_{1-6} alkylcarbonyl, Hetcarbonyl, pyrrolidiny, piperidiny, homopiperidiny, C_{3-7} cycloalkyl or C_{1-10} alkyl substituted with N(R⁶)₂ and optionally with another substituent; R³ is hydrogen, hydroxy, C_{1-6} alkyl, C_{1-6} alkyloxy, aryl C_{1-6} alkyl or aryl C_{1-6} alkyloxy, R⁴ is hydrogen, C_{1-6} alkyl or aryl C_{1-6} alkyl; R^{5a}, R^{5b}, R^{5c} and R^{5d} are hydrogen or C_{1-6} alkyl; or R^{5a} and R^{5b}, or R^{5c} and R^{5d} taken together from a bivalent radical of formula $-(\text{CH}_2)_t-$ wherein S is 4 or 5; R⁶ is hydrogen, C_{1-6} alkyl, formyl, hydroxy C_{1-6} alkyl, C_{1-6} alkylcarbonyl or C_{1-6} alkyloxycarbonyl; aryl is optionally substituted phenyl; Het is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl; as respiratory syncytial virus replication inhibitors; their preparation, compositions containing them and their use as a medicine.

WO 01/00615 A1



(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

— Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

Published:

— With international search report.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.